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## Dear Jacques:

Thank you for the culture of "W-1301-1", received here only yesterday, and for your letters of April laand 2, which arrived earlier but while I was away at Bethesda (where your own visit had made a Beting impression!) I must admit my sincere respect for your conscientious letter of the 2d. I do not, however, believe there is any moral issue involved at all; had you chosen not to send your culture, I could not criticize you for it ("Judge not lest ye be judged" according to Scripture"), but I am delighted at this indication of your interest in a collaborative approach, such as you had suggested during our very pleasant meeting here at Madison.

Perhaps some embarrassment could have been prevented had I sent some cultures by Air rather than Surface Mail, as I did on March 23. I hope you will have received them by now— they were W-2417, as explained with the package, and W-478, which is, of course, M-V<sub>1</sub>P Het. I hope you will not have too many difficulties with the latter. It is not as fruitful, as it seems, as it was at first, but should still be entirely workable. We have still not clarified all of the peculiarities of elimination in the non-disjunction stocks, and you will have to anticipate that such markers as Mal, S, Lp, and some Gal factors but not others, will invariably be found in hemizygous condition, usually retaining the markers from the F- parent, but often enough from the F+ or from both. Also, as recounted especially in my paper in the 1951 CSH, any other marker is likely to be found occasionally in the homozygous rather than heterozygous state, so that each diploid must be regarded as a personality of itself.

As to "W-1301/1", there has been time only for a first plating on EMB lactose. In my hands this culture is distinctly lactose-positive, albeit considerably weaker than wild type. Some colonies seemed to ferment more weakly than others; these will be sorted out and tested for constitutive activity. It seems to me possible that Lac<sub>1</sub> may accentuate the effect of lactose in inhibiting the constitutive formation of lactase, as can readily be tested. I am not surprised that the stock is lactose-positive for the following reasons:

- 1) Boris has retested the activation factor of Lac, induced by methyk galactoside, and found it high, but not abnormally so. This revalidates my older experiment with butyl-galactoside induction, on which some doubt was cast (in a past-card that I hope you received at Berkeley) on the possibility that the released butanol may have activated.
- 2) I had a chance to study my older experimental notes and found some forgotten fragments. You will recall that Cst acts as a partial suppressor

of Lac3. I had prepared a Lac3, and by selection on lactose had secured as a suppressor "reversion" which was a weak lactose-positive, but still glucose negative. This was then used in crosses to test whether the auppressor was separable from Lac. No Lac- Glu+ were found among several hundred prototrophs of the backcross to wild type, which was the basis of the conclusion that pt "Cst" (or at least this suppressor!) was very closely linked to Lac1. Unfortunately, the cultures seem to have been discarded before they were adeq/uately testsed for constitutive activity. At any rate, we have again taken up this approach for evaluating the incidence and genetic behavior of the Cst mutation. [Would you agree to rename this Lac, with alleles Lacci and Lacco, or some similar arrangement?

If a reprint of the constitutive paper was sent, I appear to have lost it, and would greatly appreciate another.

With best wishes from all of us,

Yours sincetely,

Joshua Lederberg